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| 08/455,426 | 05/31/95 | BARNIKOL W | DT-1216 |

18N2/1213

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| EXAMINER | |
|---|---|
| GUPTA, A | |
| ART UNIT | PAPER NUMBER |
| 1811 | 8 |

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

DATE MAILED: 12/13/96

■ This application has been examined ■ Responsive to communication filed on 10-03-96 ■ This action is made final.

A shortened statutory period for response to this action is set to expire 3 MONTHS from the date of this letter.
Failure to respond within the time period will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENTS ARE PART OF THIS ACTION:

1. ■ Notice of References Cited by Examiner, PTO-892.
2. □ Notice re Patent Drawing, PTO-948.
3. □ Notice of Art Cited by Applicant, PTO-1449
4. □ Notice of Informal Patent Application, Form PTO-152.
5. □ Information on How to Effect Drawing Changes, PTO-1474.
6. □ _____

Part II SUMMARY OF ACTION

1. ■ Claims 6-10 are pending in the application.
   Of the above claims, ____ are withdrawn from consideration.
2. □ Claims ____ have been cancelled.
3. □ Claims ____ are allowed.
4. ■ Claims 6-10 are rejected.
5. □ Claims ____ are objected to.
6. □ Claims ____ are subject to restriction or election requirement.
7. □ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. □ Formal drawings are required in response to this Office action.
9. □ The corrected or substitute drawings have been received on ____. Under 37 C.F.R. 1.84 these drawings are □ acceptable. □ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. □ The proposed additional or substitute sheet(s) of drawings, filed on ____ has (have) been □ approved by the examiner. □ disapproved by the examiner (see explanation).
11. □ The proposed drawing correction, filed on ____ has been □ approved. □ disapproved (see explanation).
12. □ Acknowledgment is made of the claim for priority under 35 USC 119. The certified copy has □ been received □ not been received □ been filed in parent application, serial no. ____; filed on ____.
13. □ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. □ Other

**EXAMINER'S ACTION**

08/455,426

SUBSTITUTE PTOL-326

## DETAILED ACTION

### *Claim Objections*

1. Claim 8 is objected to because of the following informalities: The term Glutaraldehyde is misspelled. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

2. Claims 1 and 5 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

The claims is drawn to the use of an electrolyte buffer system used as a solvent. However, it is unclear as to what step this solvent is used in. Is it used in the fractionating chromatography step or partial fractionation dissolution step?

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Potzschke et al..

The claims are drawn to a method of preparation of molecularly uniform hyperpolymeric hemoglobin wherein the method comprises as performing *at least one of the steps* of either fractional precipitation in $(NH_4)_2SO_4$ or fractionating chromatographically, or performing a partial fractional dissolution of the solution. The method further comprises the addition of a crosslinking agent such as glutaraldehyde.

The reference teaches the crosslinking of hemoglobin with glutaraldehyde and then purifying the product with sephaacryl s-400 high resolution gel (see Materials and Methods).

### *Claim Rejections - 35 USC § 103*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Potzschke et al. in view of Bonhard et al.

The claims are drawn to a method of preparation of molecularly uniform hyperpolymeric hemoglobin wherein the method comprises as performing, at least one of the steps or all of the steps in any order, of either fractional precipitation in $(NH_4)_2SO_4$ or fractionating chromatographically, or performing a partial fractional dissolution of the solution. The method further comprises the addition of a crosslinking agent such as glutaraldehyde.

The reference teaches the crosslinking of hemoglobin with glutaraldehyde and then purifying the product with sephaacryl s-400 high resolution gel (see Materials and Methods). The disclosed method initially wash the hemoglobin with an electrolyte I solution (NaCl, KCl, $NaHCO_3$, and $NaN_3$), then crosslink the hemoglobin with glutaraldehyde, then purifying the product with Sephacryl S-400 high resolution gel with a NaCl, HEPES buffer, and $NaN_3$ as the eluent electrolyte solution. The difference between the reference and the instant application is that the reference does not teach the process of fractional precipitation with $(NH_4)_2SO_4$.

However, the reference of Bonhard et al. teach a method of cross-linking the hemoglobin solution and then diminishing the amount of uncross-linked hemoglobin by the use of Ammonium Sulfate solution (see col.

3, lines 25-35). Therefore it would have been obvious to one of ordinary skill in the art to use Ammonium Sulfate solution because this solution would precipitate any uncrosslinked-hemoglobin remaining and thus obtaining a purer crosslinked product.

As to the specific concentrations claimed, generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller , 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40C and 80C and an acid concentration between 25 and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100C and an acid concentration of 10%.). See also In re Hoeschele , 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc. , 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied , 493 U.S. 975 (1989), and reversing the order of the chromatographic steps.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (703) 308-0254. The fax phone number of this group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

CECILIA J. TSANG
SUPERVISORY PATENT EXAMINER
GROUP 1800